GARDASIL™

[Quadrivalent Human Papillomavirus (Types 6,11,16,18) Recombinant Vaccine]

An Analysis of Disease Burden, Efficacy, in North American Women

Presentation Outline

GARDASIL™
[Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine]

- Approach to Evaluation of Population Impact
- Cross-sectional prevalence data in North America
- Efficacy in the North American population

GARDASIL® is a Prophylactic HPV Vaccine

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- Subjects who are naïve to all 4 vaccine HPV types derive maximum benefit **(Naïve)**
- Subjects with ongoing/prior infection with <4 vaccine HPV types derive some benefit **(Partially Exposed)**
- Subjects with ongoing/prior infection with 4 vaccine HPV types derive little benefit **(Fully Exposed)**

The U.S. Population Contains a Mix of Naïve, Partially Exposed, and Fully Exposed Women

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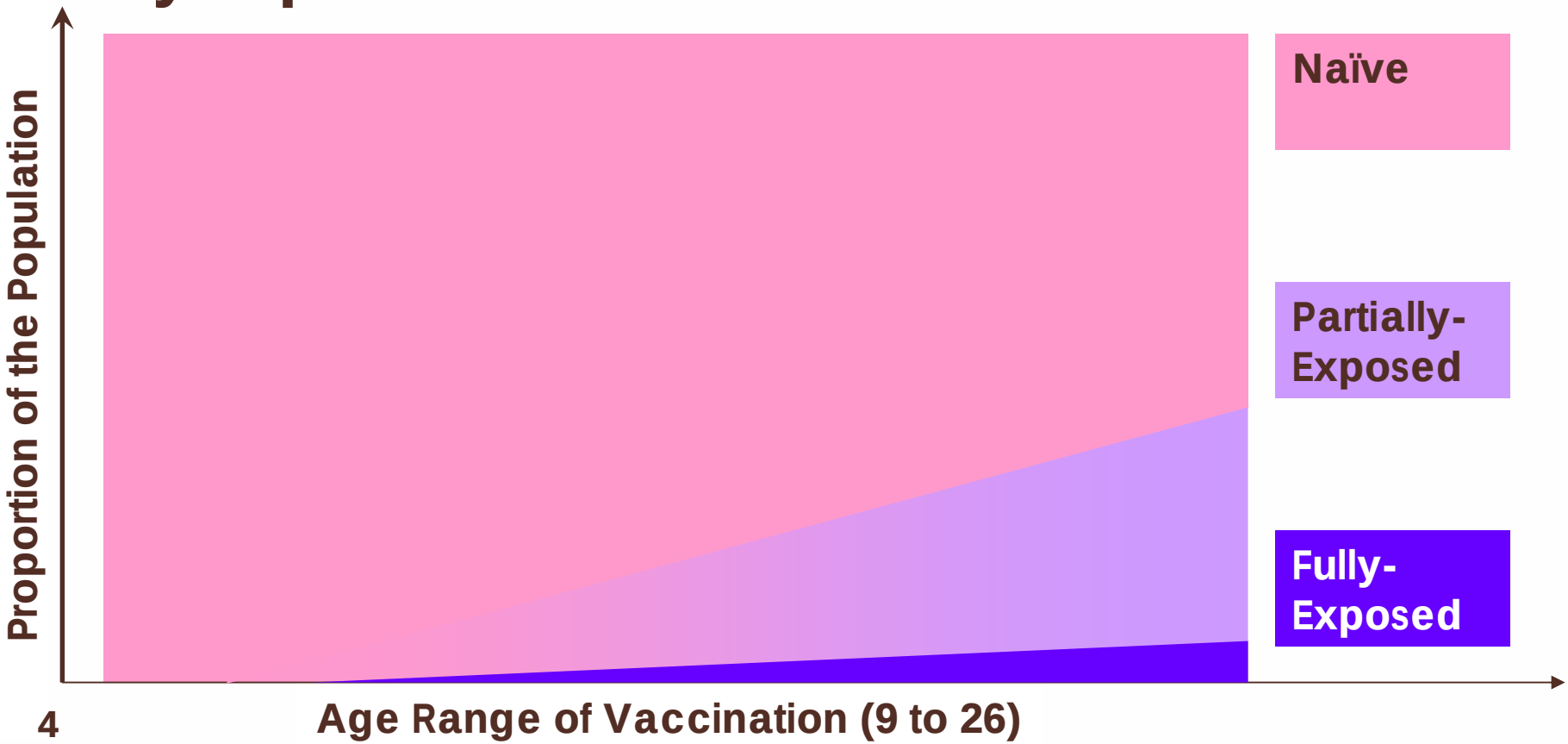

- Population benefit decreases over age range, but **almost all subjects derive some benefit**
- For cost-effectiveness calculations, **value of prevention increases after sexual debut** (faster time to infection and accrual of costs)

Clinical Studies of GARDASIL®
North American Women (N=5996)

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- **Inclusion criteria (16-24 Year Old Women)**
  - Lifetime sex partners (insertive intercourse) at Day 1
    - Phase IIa: <6; Phase IIb/III: <5
    - Virginal 16-17 year-olds not allowed to enroll
  - Prior to Day 1, no history of an abnormal Pap or CIN

- **Clinical study sites**
  - Most sites on college campuses
  - Several sites in inner city settings

- **Enrollment of subjects regardless of Day 1 HPV status**
  - **1° evaluation: prophylactic efficacy** in baseline HPV-naïve subjects (2005)
  - **2° evaluation: general population impact** in all subjects, regardless of Day 1 HPV status (2007)
  - 2 to 4 years of follow-up

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Age/Ethnicity/Pregnancy

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16- to 24-Year-Old North American Women Enrolled in Studies of GARDASIL®

	Subjects (N = 5,996)	U.S. Census (2000)
Age (years)		
Mean (Standard Deviation)	19.9 (1.7)	
Median (Range)	20 (16 to 25)	
Race/Ethnicity		
Asian	4.7%	3.6%
Black	8.5%	12.3%
Hispanic American	10.2%	-- †
White	73.4%	75.1%
Other	3.1%	9.0%
Pregnancy History	15.4%	--

†12.5% of subjects were Hispanic (divided among white/black/other)

Sexual Behavior Parameters

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16- to 24-Year-Old North American Women Enrolled in Studies of GARDASIL®

	Subjects (N = 5,996)	NSFG (15-24 Year-Olds)
Non-virgins at Day 1	92%	77%
Mean Age at First Sexual Intercourse (Non-Virgins) (yrs)	16.9 (1.9)	--
Lifetime Number of Sex Partners at Day 1(Non-Virgins)		
1	27.1%	35.4%
2	24.7%	14.4%
3	22.9%	33.1%†
4	19.1%	
5	6.2%	
>5	0.0%	17.3%†
Median	2	2
Self Reported STI History	9.6%	11.9%

†3 to 6 Lifetime Sexual Partners

NSFG: National Survey of Family Growth

STI and Pap Test Results at Day 1

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16- to 24-Year-Old North American Women Enrolled in Studies of GARDASIL®

Mandatory Chlamydia/GC Testing (Day 1)	Subjects (N = 5,996)
Chlamydia	3.0%
Gonorrhea	0.4%

Day 1 Parameter	Subjects (N = 5,996)
Subjects with a Satisfactory Pap Test	5,912
Result Among Subjects with a Satisfactory Pap Test	
Negative for SIL	87.0%
Positive for SIL	13.0%
ASC-US or ASC-H	6.2%
LSIL	6.2%
HSIL	0.5%
AGC or AIS	0.1%

Results of HPV Testing at Day 1

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16- to 24-Year-Old North American Women Enrolled in Studies of GARDASIL® (Protocols 007, 013, 015)

Sero- and/or PCR-Positivity to HPV 6, 11, 16, or 18	Subjects (N = 3587)
Naïve to HPV 6/11/16/18	76.1%
Positive to HPV 6, 11, 16, or 18	23.9%
Positive by Serology	16.7%
Positive by PCR	13.8%
Positivity by Number of Vaccine HPV Types	
Positive to 1 or more types	23.9%
Positive to 2 types	4.8%
Positive to 3 types	1.0%
Positive to 4 types	0.1%

Positivity to HPV 16 and/or 18 by Age

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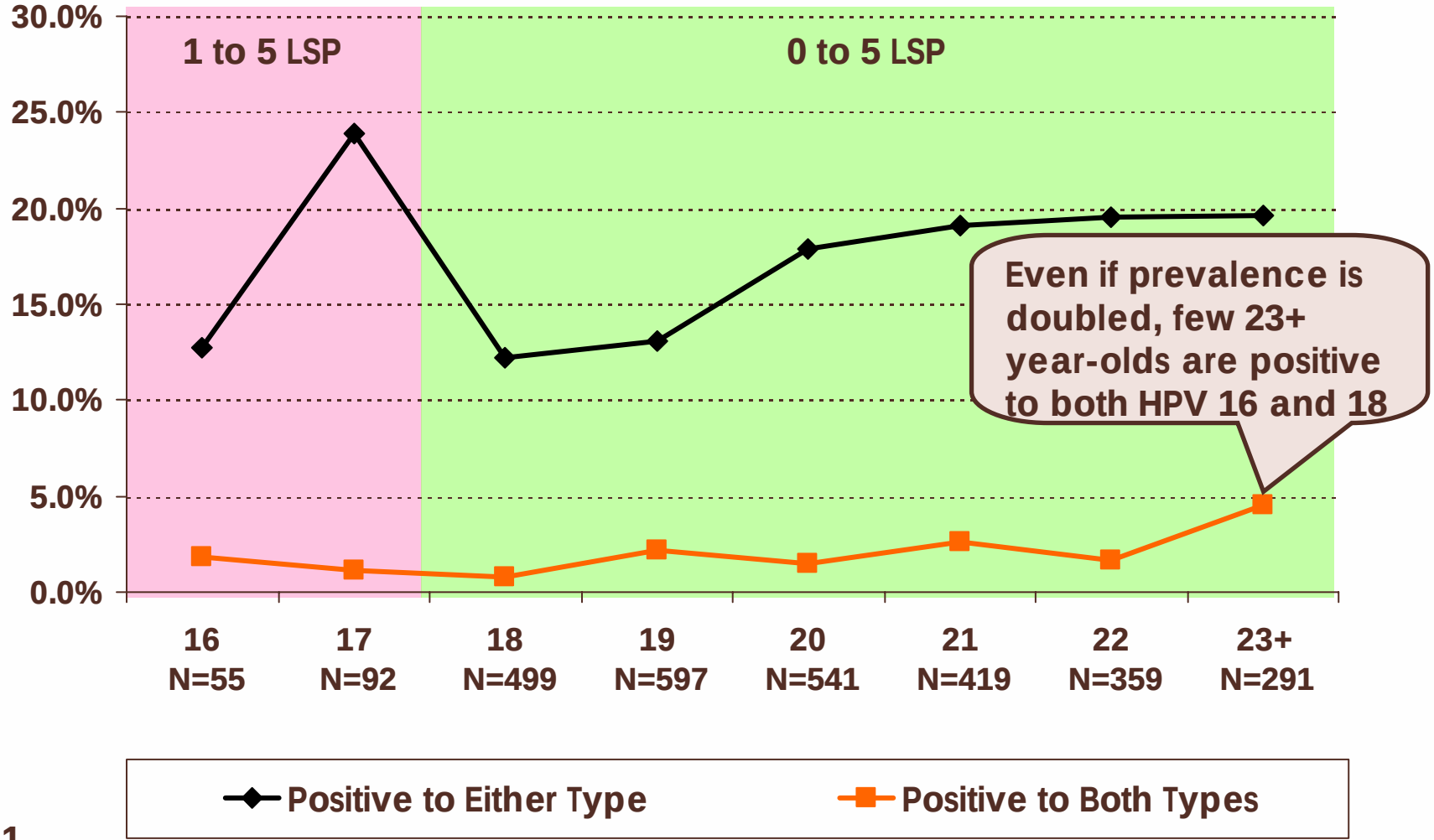

Positivity to HPV 16 and/or 18 by Pap Test Result

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16- to 24-Year-Old North American Women Enrolled in Studies of GARDASIL® (Protocol 007, 013, 015)

		HPV Status		
	Subjects	Naive to HPV 16 and HPV 18	Positive to either HPV 16 or HPV 18	Positive to both HPV 16 and HPV 18
Day 1 Pap Test Results2	N	%	%	%
Negative for SIL	2487	85	14	2
ASC-US or Worse	303	58	36	6
ASC-US (-)/No probe	92	76	21	3
ASC-US (+) or Worse	211	50	43	**7**
ASC-US HPV (+)	36	40	53	**3**
LSIL, ASC-H or Worse	175	51	41	**8**
ASC-H/AGC	5	80	0	**20**
LSIL	162	53	40	**7**
HSIL	8	0	75	**25**

N = Number of subjects who received ≥1 vaccination in the indicated Pap category with non-missing serology and PCR data for HPV 16 and HPV 18.

Positivity to HPV 16 and/or HPV 18 by Lifetime Sex Partners at Day 1

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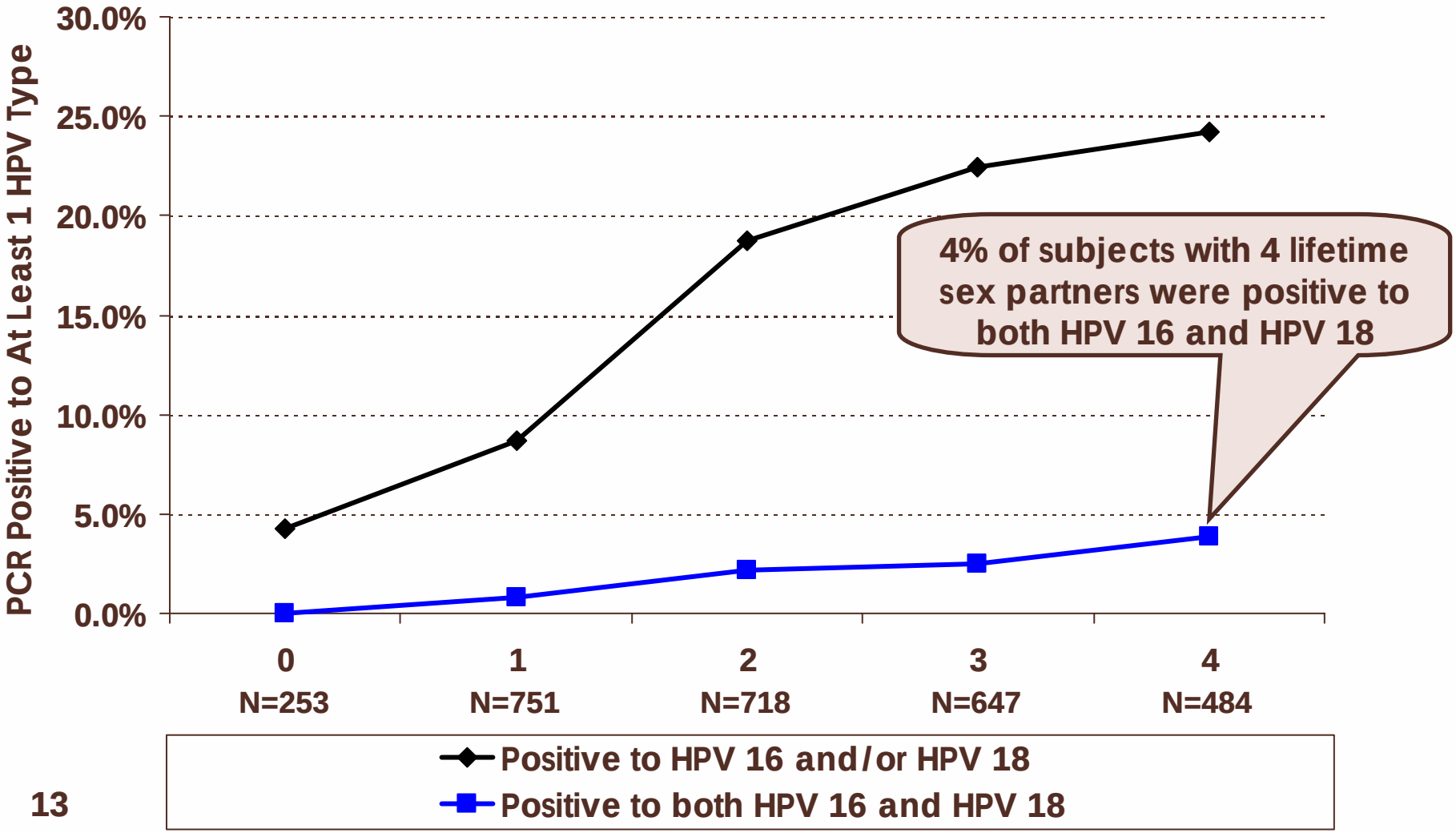

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Role of Baseline HPV Status in Endpoint Counting for Prophylactic Efficacy

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Baseline HPV Status	Clinical Endpoint			
	HPV 6	HPV 11	HPV 16	HPV 18
Naïve to all 4 Types	Yes	Yes	Yes	Yes
Positive to HPV 6 or 11 Naïve to HPV 16 and 18	No	No	Yes	Yes
Positive to HPV 16 Naïve to HPV 6, 11, and 18	Yes	Yes	No	Yes
Positive to HPV 18 Naïve to HPV 6, 11, 16	Yes	Yes	Yes	No

Prophylactic Efficacy and General Population Impact - North America

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- If naïve to HPV 16 and 18 at Day 1, efficacy for HPV 16/18 disease
- If naïve to HPV 18 (but HPV 16+) at Day 1, efficacy for HPV 18 disease
- If naïve to HPV 16 (but HPV 18+) at Day 1, efficacy for HPV 16 disease

Endpoints	Analysis	GARDASIL or HPV 16 Vaccine	Placebo	% Reduction (95% CI)
HPV 16/18-related CIN 2/3 or AIS	HPV-Naïve Efficacy			
	HPV 16(+) and/or 18(+) at Day 1			
	General Population Impact			

- Vaccine Impact in all subjects, regardless of baseline HPV status

- If positive to HPV 16 at Day 1, impact on disease caused by HPV 16
- If positive to HPV 18 at Day 1, impact on disease caused by HPV 18

Prophylactic Efficacy and General Population Impact - North America

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Endpoints	Analysis	GARDASIL or HPV 16 Vaccine	Placebo	% Reduction (95% CI)
HPV 16/18-related CIN 2/3 or AIS	HPV-Naïve Efficacy	0	30	100 (87, 100)
	HPV 16(+) and/or 18(+) at Day 1	17	22	--
	General Population Impact	17	52	67 (42, 82)

Population Impact of GARDASIL® HPV 6/11/16/18-Related CIN 2/3 or AIS

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General North American Population of Protocols 005, 007, 013, and 015†

Group	HPV Vaccine Cases/ 100 Pyr	Placebo Cases/ 100 Pyr	% Reduction	95% CI
Overall	0.3	0.8	67	42, 82
Age (Years)				
<19	0.4	0.8	51	<0, 87
19 to 21	0.2	0.9	72	40, 88
>21	0.2	0.6	67	<0, 94
Lifetime Sex Partners				
0	0.2	1.0	75	<0, 100
1 to 3	0.3	0.7	64	26, 84
4+	0.3	1.1	69	14, 91
Pap Test Result				
Negative for SIL	0.1	0.8	85	65, 95
SIL Present	1.1	1.1	7	<0, 65

† Protocol 005 – HPV 16 endpoints only; Protocol 013 – HPV 16 arm excluded.

Time to Detection
HPV 16/18-Related CIN 2/3 or AIS
General Population in North America

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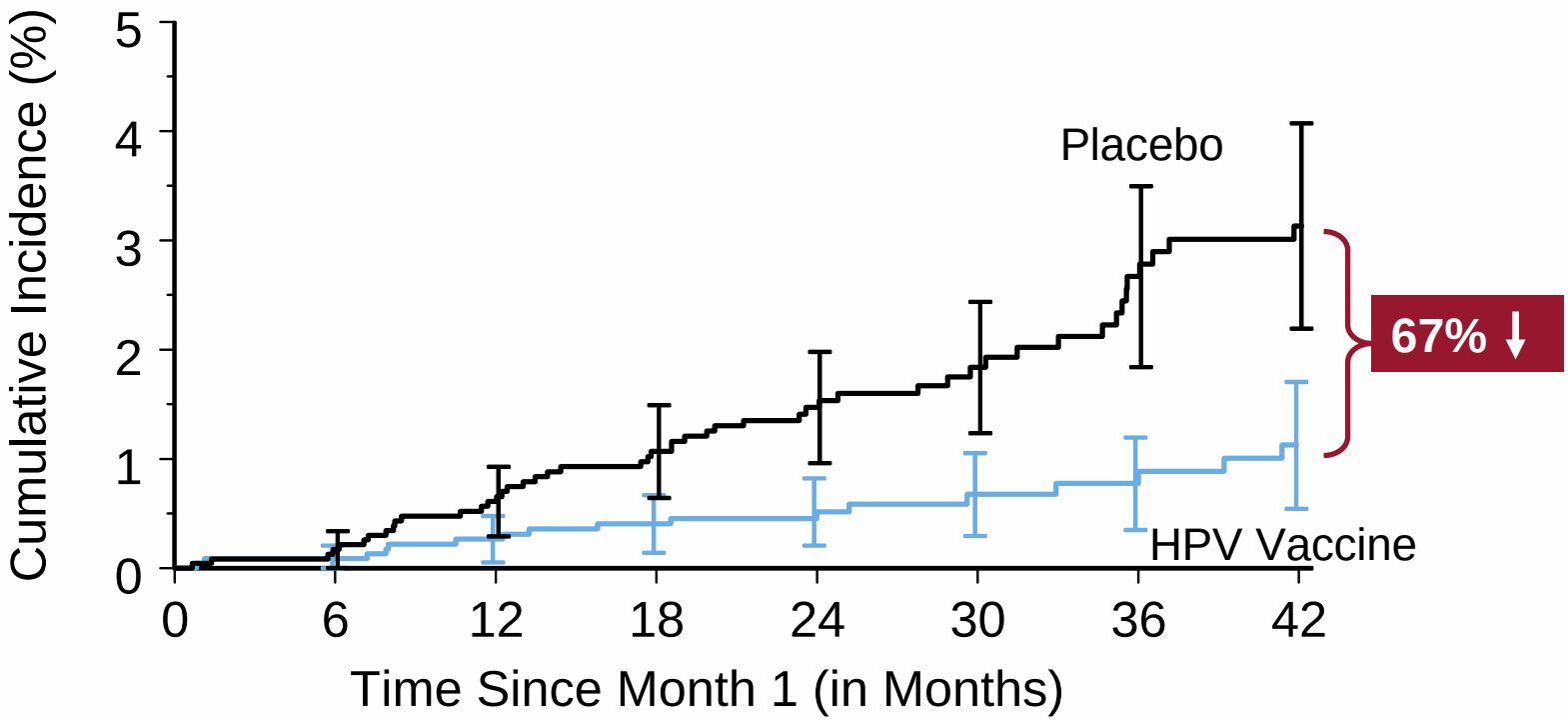
(Protocols 005, 007, 013, and 015 Combined)



Number of Subjects at Risk

HPV Vaccine	2307	2254	2155	2095	1529	1063	880	816
Placebo	2354	2306	2199	2122	1547	1098	857	800

Population Impact of GARDASIL®
CIN 2/3 or AIS

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General North American Population of Protocols 005, 007, 013, and 015

Group	HPV Vaccine Cases/ 100 Pyr	Placebo Cases/ 100 Pyr	% Reduction	95% CI
Overall	1.0	1.4	32	5, 52
Age (Years)				
<19	1.5	1.5	<0	<0, 49
19 to 21	1.9	1.4	39	3, 62
>21	0.8	1.5	48	<0, 78
Lifetime Sex Partners				
0	0.2	1.0	75	<0, 100
1 to 3	1.0	1.3	22	<0, 49
4+	1.1	1.9	43	<0, 70
Pap Test Result				
Negative for SIL	0.6	1.1	47	16, 67
SIL Present	3.1	3.6	14	<0, 50

General Population Impact Improves With Increased Duration of Follow-Up

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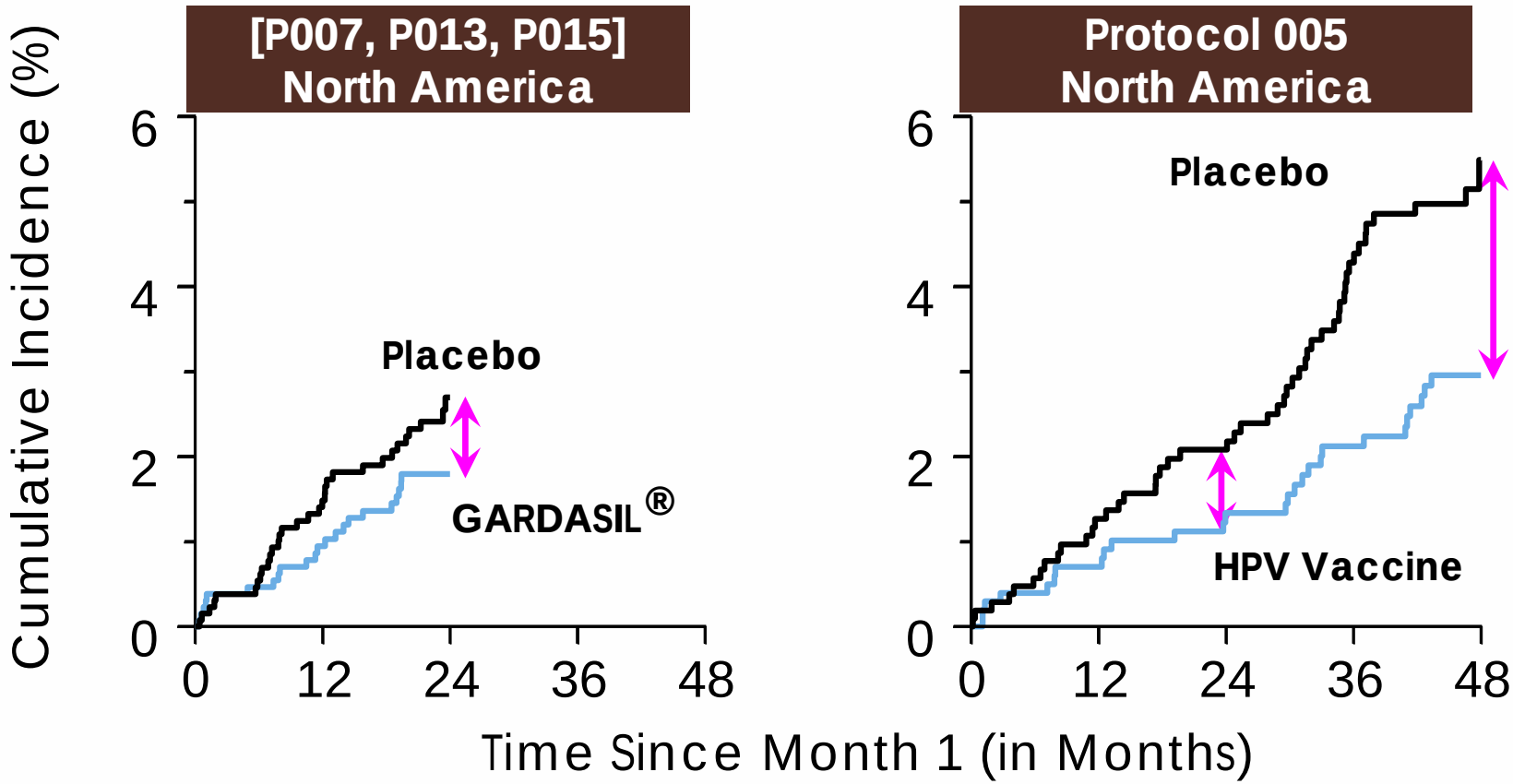

GARDASIL®	1290	1194	616		HPV Vaccine	1017	958	912	849	276
Placebo	1304	1206	603		Placebo	1050	985	939	834	246

Conclusions

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- In the general population of 16- to 24-year-old North American women
  - Most subjects are naïve to all 4 vaccine HPV types
  - Few subjects are positive to both HPV 16 and 18
    - Even with 4 LSP
    - Even with a Pap test abnormality
  - Event rates are high
- Administration of GARDASIL® is highly effective at reducing the burden of HPV disease
- Benefits of GARDASIL® become more apparent over time